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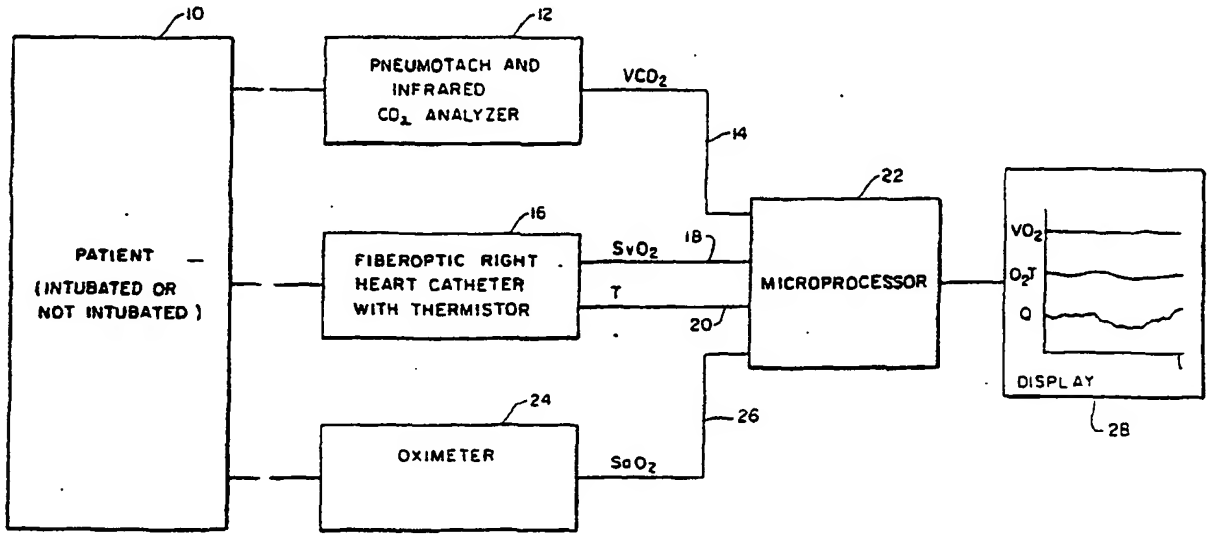

(57) Abstract

A method of continuously monitoring cardiac output of a patient (10) includes the step of determining a value of a cardiac output constant which is assumed to remain stable over the period of interest and is determined as a function of values of various measured parameters of the patient. These values may include thermodilution cardiac output (20), carbon dioxide production (14), arterial (26) and mixed venous (18) oxygen saturation and hemoglobin. Thereafter, cardiac output is continuously determined employing the calculated cardiac output constant and monitored values of carbon dioxide production and arterial and mixed venous oxygen saturation. Oxygen transport may also be monitored on a continuous basis.

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METHODS and APPARATUS for CARDIAC OUTPUT MEASUREMENT.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to the continuous measurement or monitoring of the cardiac output of the human body. Cardiac output is the volume of blood ejected by the heart per unit time. It is a useful measurement in that it can be used to evaluate overall cardiac status in critically ill patients, patients with suspected cardiovascular and pulmonary disease, and high risk patients undergoing surgery. The present invention also relates to continuous monitoring of oxygen transport. Oxygen transport is the volume of oxygen transported from the heart and lungs to the body per unit time. It is useful to assess the cardiorespiratory status of the above patients.

2. Description of the Prior Art

Cardiac output has been measured by a number of different methods. Several methods are described in Cardiac Output Measurements. A review Of Current Techniques And Research, by Ehlers et al. in the Annals Of Biomedical Engineering, Vol. 14, pp. 219-239, 1986. This publication discusses both "intermittent" cardiac output measurements for obtaining a single measurement and "continuous" measurements in which various patient parameters are continuously monitored and cardiac output calculated on a regular and repeating basis. Although high accuracy can be obtained with certain intermittent measurement techniques, it is very desirable to be able to provide continuous information regarding cardiac output. Currently, the most popular technique for measuring cardiac output intermittently is via an indicator dilution method, and particularly thermodilution. In indicator dilution techniques, a

predetermined amount of substance is introduced at a single point in the bloodstream and analyzed at a point downstream to obtain a time dilution curve. The average volume flow is inversely proportional to the integrated area under the dilution curve. In the thermodilution method, the indicator is a temperature change of the blood. The temperature change is typically produced by injecting cold saline through a catheter into the right atrium. This results in a cooling of the blood, which is measured at a downstream location with the same catheter to produce a thermodilution curve. Cardiac output can then be determined. This technique employs a catheter with a thermistor at the tip.

Other methods of cardiac output measurement are based upon the Fick principle. According to this principle, the rate of uptake or release of a substance to or from blood at the lung is equal to the blood flow past the lung and the content difference of the substance at each side of the lung. This can be expressed by the equation:

$$\text{Uptake} = Q\,(c_2 - c_1),$$

where Q is the blood flow (cardiac output), c_2 the content of the substance leaving from the lung and c_1 the content of the substance coming to the lung. Applying this relationship to oxygen yields:

$$Q = VO_2/(c_aO_2 - c_vO_2), \qquad (1)$$

where VO_2 is the volume of oxygen inspired per unit time and c_aO_2 and c_vO_2 are respectively the arterial and mixed venous oxygen contents. Applying the relationship to carbon dioxide yields:

$$Q = VCO_2/(c_vCO_2 - c_aCO_2), \qquad (2)$$

where VCO_2 is the volume of carbon dioxide produced by the patient per unit time and c_vCO_2 and c_aCO_2 are

respectively the mixed venous and arterial carbon dioxide contents. Determination of VO_2 and VCO_2 require a volume measurement (e.g., via integration of a flow signal or via a rotameter) and a fractional concentration measurement (e.g., via mass spectrometer or gas analyzer (infrared or polarographic)).

The Fick method is most commonly used with oxygen as the analyzed substance. Equation (1) has been used to obtain intermittent measurements of Q. Via indwelling catheters, arterial and venous blood samples were obtained and these samples were analyzed on a blood gas analyzer to obtain the oxygen saturation (SO_2) and the partial pressure of oxygen (PO_2). Arterial and venous oxygen contents were then calculated from the formula:

$$cO_2 = 1.34 \cdot Hgb \cdot SO_2 + 0.0031 \cdot PO_2, \quad (3)$$

where Hgb is the hemoglobin in gm/100ml of the patient, SO_2 is in percent, cO_2 is in ml of O_2/100ml of blood, and 1.34 is a constant in ml/gm (other values of this constant, e.g., 1.36 and 1.39 have also appeared in the literature). The above approach only yields intermittent measurements and is also cumbersome. Therefore, it is typically not used in critically ill patients.

The dissolved oxygen ($0.0031 \cdot PO_2$) in equation (3) is generally negligible so that equation (1) can be simplified to:

$$Q = VO_2/(13.4 \cdot Hgb \cdot (S_aO_2 - S_vO_2)) \quad (4)$$

where Q is in l/min, VO_2 in ml/min, Hgb in gm/100ml and S in percent. S_aO_2 can be measured continuously via an oximeter (pulse, transmission or indwelling type). Similarly, S_vO_2 can be measured continuously via reflectance oximetry and a fiberoptic pulmonary artery (right heart) catheter. Several systems have been developed to continuously monitor cardiac output via

continuous measurement of VO_2, S_aO_2 and S_vO_2. Such methods are described in Hankeln, et al. Continuous, On-line, Real-Time Measurement of Cardiac Output and Derived Cardiorespiratory Variables in the Critically Ill. Crit. Care Med 13, 1071, 1985; Davies, et al. Continuous Fick Cardiac Output Compared to Dilution Cardiac Output. Crit. Care Med 14, 881, 1986; and Tachimori, et al. On-line Monitoring System for Continuous and Real-Time Cardiac Output. Crit Care Med (Abstract) 14, 401, 1986. The methods described provide fairly good results; however, oxygen Fick methods all have the common drawback that it is difficult to measure the body's rate of oxygen uptake accurately. This is particularly so when the patient is inspiring a high concentration of oxygen (FIO_2), as occurs frequently in critically ill patients. In addition, FIO_2 can vary from breath to breath in patients on ventilators (this occurs because of inaccuracies in the internal blender or pressure fluctuations in the oxygen and air supply). VO_2 measurement is therefore difficult in ventilator dependent patients unless a blender external to the ventilator or calibrated gases from an external tank are used. Furthermore, patients may be on various modes of ventilation such as flow-by, where part of the oxygen bypasses the patient's mouth. In this situation, complicated valving is required to separate the patient's exhaled gas from the flow-by gas. It is therefore difficult to provide a universally applicable system for VO_2 measurement.

The difficulty of VO_2 measurement at high oxygen concentration is recognized in the Davies et al publication and is theoretically discussed in Ultman, et al., Analysis of Error in the Determination of Respiratory Gas Exchange at Varying F_IO_2, J Appl Physiol 50, 210, 1981. The Davies publication mentions approximating the VO_2 by measuring carbon dioxide output (VCO_2) and dividing it by an assumed respiratory quotient RQ. This method has the potential disadvantage that the assumed value of the respiratory quotient of the patient may be incorrect.

The Fick method has also been applied to carbon dioxide employing equation (2) to obtain intermittent cardiac output. The c_vCO_2 is usually estimated from the partial pressure of carbon dioxide (P_vCO_2). The latter may be obtained indirectly by breath holding or more popularly by rebreathing. Such methods are described in Davis, C.C., et al. Measurements of Cardiac Output in Seriously Ill Patients Using a CO_2 Rebreathing Method. Chest 73, 167, 1978; and Blanch, et al., Accuracy of an Indirect Carbon Dioxide Fick Method in Determination of the Cardiac Output in Critically Ill Mechanically Ventilated Patients, Int. Care Med 14, 131, 1988. A major disadvantage of this method is that it yields only intermittent values of Q since the partial pressure of carbon dioxide is estimated via rebreathing. More recently, a partial rebreathing method that does not require monitoring of P_vCO_2 has been used in dogs (Capek, et al., Noninvasive Measurement of Cardiac Output Using Partial CO_2 Rebreathing. IEEE Trans. Biomed. Eng. 35, 653, 1988). This method is also intermittent and it is unlikely that it can be easily applied to patients with lung disease.

SUMMARY OF THE INVENTION

The present invention is directed to a method and apparatus for continuously monitoring cardiac output by utilizing a modified Fick equation. In order to eliminate the inaccuracies associated with monitoring the rate of uptake of oxygen, however, VO_2 in the oxygen Fick equation is replaced by VCO_2 divided by a constant representative of the gas exchange ratio of a patient. This ratio is assumed to remain constant over the measurement period of interest. The value of the constant is determined for the patient by initially measuring at least one patient parameter and making a determination of the constant based upon the measured parameter. In one embodiment, an initial cardiac output determination employing a technique such as thermodilution is performed and initial values of arterial and mixed venous oxygen saturation and CO_2 production for the patient are obtained. The obtained values are inserted into the modified Fick equation in order to obtain a value of a constant, referred to as a "cardiac output constant". Subsequently, the volume of carbon dioxide expired by the patient and mixed venous oxygen saturation content are continuously monitored, and cardiac output is calculated in real time from the current monitored values and the previously determined cardiac output constant. The initial arterial oxygen saturation value may be used in the modified Fick equation for certain patients in which arterial oxygen saturation remains substantially constant. For other patients, the arterial oxygen saturation content is continuously monitored and the current value inserted into the modified Fick equation. Hemoglobin may be monitored on an intermittent or continuous basis or may be assumed to be a constant value and be included in the cardiac output constant. Real time output can be combined with the simultaneously obtained oxygen saturation to yield real time oxygen transported to the tissues. The invention can provide significant improvements in continuous cardiac output and oxygen transport measurement by relying upon measurements of carbon dioxide production rather than oxygen consumption.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be described with reference to the accompanying drawings, wherein:

Figure 1 is a block diagram of the present invention; and

Figure 2 is a block diagram illustrating the method of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The following description is of the best presently contemplated mode of carrying out the invention. This description is made for the purpose of illustrating the general principles of the invention and is not to be taken in a limiting sense. The scope of the invention is best determined by reference to the accompanying claims.

As discussed above, the oxygen Fick equation is represented in general form by the following:

$$Q = VO_2/(c_aO_2 - c_vO_2). \qquad (1)$$

By ignoring the dissolved oxygen content expressed in equation (3), the above oxygen Fick equation can be represented as:

$$Q = VO_2/(13.4 \cdot Hgb \cdot (S_aO_2 - S_vO_2)) \qquad (4)$$

The present invention relies on the postulate/observation that during the steady state the gas exchange ratio, R, for carbon dioxide and oxygen is constant:

$$R = VCO_2/VO_2 = \text{constant} \qquad (5)$$

The value of this constant depends primarily on the fuel mixture (e.g., fat, protein or carbohydrate) that the body is metabolizing. The present invention is based upon the assumption that R will not vary significantly over the time period of interest (e.g., a number of hours). Research has provided evidence that this is valid over 24 hours at least with respect to critically ill patients (see. e.g. van Lanschot, et al. Accuracy of Intermittent Metabolic Gas Exchange Recordings Extrapolated for Dinural Variation. Crit. Care Med. 16, 737, 1988.) R may therefore be considered constant and VO_2 in equation (4) may be replaced by VCO_2/R. This yields the following:

$$Q = VCO_2/(13.4 \cdot Hgb \cdot R \cdot (S_aO_2 - S_vO_2)) \quad (6)$$

This is of the form:

$$Q = VCO_2/(k \cdot (S_aO_2 - S_vO_2)), \quad (7)$$

where k is a constant ($k = 13.4 \cdot Hgb \cdot R$) and the variables are functions of time.

From equation (7), Q can be determined and measured continuously if k is known and if VCO_2, S_aO_2 and S_vO_2 are continuously monitored. In the preferred embodiment of the present invention, k is determined by making an initial cardiac output determination with another technique, such as thermodilution. At a time zero, Q, VCO_2, S_aO_2, and S_vO_2 are measured. A hemoglobin measurement may also be made from a blood sample of the patient. Substituting these initial values of Q, VCO_2, S_aO_2 and S_vO_2 in equation (7) yields k. Q may thereafter be continuously determined by monitoring VCO_2, S_aO_2 and S_vO_2.

Referring to Figure 1, a patient is indicated at 10. Various continuous monitoring devices are coupled to the patient in order to facilitate the continuous cardiac output measurement of the present invention. Each of these devices is commercially available. The volume of carbon dioxide expired by the patient is monitored by means of a volumetric analyzer 12 which includes, for example, a pneumotach and infrared CO_2 analyzer along with appropriate processing circuitry. An output signal is provided on line 14 representative of the volume of carbon dioxide expired by the patient per unit time (e.g., ml/min). This measurement is averaged over time intervals sufficient to filter out rapid fluctuations and thus provides an accurate representation of volume of carbon dioxide expired by the patient. The unit 12 may, for example, be comprised of a Beckman MMC Horizon System which provides an output of carbon dioxide production in ml/min. Such an output is also provided by a Waters Instruments, Inc. MRM-6000 metabolic analyzer.

A fiberoptic pulmonary (right heart) catheter 16 including a thermistor is employed to monitor mixed venous oxygen saturation and to perform the initial thermodilution cardiac output measurements. Several fiberoptic right heart catheters are commercially available, and may include circuitry to provide an output signal representative of mixed venous oxygen saturation S_vO_2, expressed as a percentage. This output is indicated on line 18 in Figure 1. An Oximetrix Model IX catheter providing a continuous output signal representative of S_vO_2 may be employed. This unit includes a catheter and oximetry processor (Oximetrix 3 SO_2/cardiac output computer, Abbott Labs, Mountain View, CA.) to provide the S_vO_2 signal. Other units, such as an Edwards S_vO_2/cardiac output unit (SAT 2, Baxter Edwards, Irvine, CA.) with an Edwards venous oximetry catheter, could also be used.

The right heart catheter 16 includes a thermistor to provide a temperature signal for use in calculating an initial cardiac output by means of the thermodilution technique. The temperature output of the thermistor is provided on line 20 to a microprocessor system 22 which is employed to calculate thermodilution cardiac output Q_{TD} by employing a known thermodilution cardiac output equation (such as that disclosed in Ehlers et al, supra). The thermodilution cardiac output as determined by the microprocessor 22 is employed to determine the cardiac output constant as discussed below. (It should be noted that the catheter unit may include its own processing circuitry, in which case the output to the processor 22 would be a calculated value of Q_{TD} rather than temperature.)

An oximeter 24, which may be a pulse, transmission, reflectance or indwelling type, is employed to monitor arterial oxygen saturation of the patient 10. The oximeter 24 provides an output signal on line 26 indicative of arterial saturation percentage. In one embodiment, an Ohmeda Biox 3740 pulse oximeter is employed to provide the S_aO_2 signal.

Thus, the microprocessor 22 receives continuous signals indicating the value of VCO_2, S_vO_2 and S_aO_2 on lines 14, 18 and 26, respectively. In addition, temperature measurements are received on line 20 to facilitate the initial thermodilution cardiac output determination (and possible subsequent determinations if updating is desired).

The method for continuously measuring cardiac output in conjunction with the system of Figure 1 is illustrated in Figure 2. When it is desired to begin measuring cardiac output, several thermodilution cardiac outputs Q_{TD} are obtained by employing the known thermodilution technique. An average Q_{TD} is then determined. Initial values of VCO_2, S_vO_2 and S_aO_2 are obtained from the units 12, 16 and 24, respectively. In addition, a value of the patient's hemoglobin Hgb is obtained by blood sample analysis. These initial measurements are indicated at 40 in Figure 2. Once the initial values are obtained, the value of R in equation (6) and the value of k in equation (7) can be calculated by the microprocessor 22. This is indicated at box 42 in Figure 2.

Once the value of k has been determined, continuous determination of cardiac output is facilitated by monitoring the VCO_2, S_vO_2 and S_aO_2 signals on lines 14, 18 and 26. That is, the microprocessor 22 can continuously calculate Q based upon equation (7) employing the previously calculated value of k. This is indicated at boxes 44 and 46 of Figure 2. The calculated value of Q may be displayed over time (Q(t)) by means of a display 28 shown in Figure 1 and indicated at Box 48 in Figure 2. In this embodiment, it is assumed that the value of k (which includes R and Hgb) for a patient will remain substantially constant for the time period of interest (e.g., a 24 hour period), and it is therefore sufficient to perform only one thermodilution cardiac output determination (typically the average of several measurements closely spaced in time) at the beginning of

this time period in order to calculate k. However, k and R may be repeatedly updated by performing the initialization procedure in step 40 (Figure 2) at any desired times (e.g., each 4 hours). During these intervals Q(t) may be displayed as described above and in Figure 2.

The use of the measured values of VCO_2, S_vO_2 and S_aO_2 to calculate k and subsequently calculate Q has the further advantage that any instrumentation offsets associated with these measurements are compensated for in the calculated value of k. It is therefore preferable to employ these parameters in determining k. However, the invention is not so limited. R or k may be determined by other methods. For example, in addition to the VCO_2 measurement obtained by the unit 12, VO_2 may be measured (by using the Beckman MMC Horizon System, for example) and R calculated from equation (5). Arterial and venous blood sampling may also be used to determine R. Combining equations (1) and (2) yields:

$$R = (c_vCO_2 - c_aCO_2)/(c_aO_2 - c_vO_2) \qquad (8),$$

so that R can be determined from the arterial and venous oxygen and carbon dioxide contents.

Alternatively, VO_2 may be calculated via equation (1) from the initial cardiac output measurement Q and measured (e.g., via blood sampling) arterial and venous oxygen contents. Use of this VO_2, together with the simultaneously measured VCO_2, in equation (5) yields R.

In each implementation of the present invention, at least one initial parameter of the patient is measured and a cardiac output constant is determined. This constant is then used in the modified Fick equation in order to enable continuous measurements of cardiac output to be obtained by monitoring VCO_2, S_vO_2 and S_aO_2 (and Hgb if desired). By enabling measurements to be made based upon carbon dioxide production as opposed to oxygen uptake, accurate and consistent continuous cardiac output measurements may be obtained.

Since R is determined by an initial thermodilution measurement of cardiac output and CO_2 production is monitored continuously thereafter, it is possible to employ equation (5) to continuously monitor oxygen uptake, VO_2. This value may be calculated by the microprocessor 22 and displayed on the display unit 28. Similarly, oxygen transport of the patient may be calculated in accordance with the following:

$$O_2T = 10 \cdot c_aO_2 \cdot Q(t) = 13.4 \cdot Hgb \cdot S_aO_2 \cdot Q(t), \quad (9)$$

where O_2T is the oxygen transported by the heart to the body in ml/min. The real time calculated value may be displayed by the unit 28. Other patient parameters, such as oxygen extraction ratio (VO_2/O_2T) may also be continuously monitored. The initial determination of R and subsequent real time monitoring of VCO_2, S_aO_2 and S_vO_2 thus facilitates monitoring of various parameters in addition to cardiac output.

When employing equation (7) to determine Q, the patient's hemoglobin is assumed to remain constant and is therefore included in the value of the calculated cardiac output constant k. However, more accurate determination of Q is facilitated by treating hemoglobin as a variable and monitoring its value either intermittently or continuously. In this case, the equation for determining cardiac output is as follows:

$$Q = VCO_2/(k' \cdot Hgb \cdot (S_aO_2 - S_vO_2)), \quad (10)$$

where k' is equal to 13.4·R, from equation (6). Values for Hgb are provided to the microprocessor 22 in this embodiment along with the values of VCO_2, S_vO_2 and S_aO_2. The value of the constant k' is then determined (like k) from the initial values of Q, Hgb, S_aO_2 and S_vO_2. Once k' is determined Q may be monitored in real time from the values of VCO_2, Hgb, S_aO_2 and S_vO_2.

Although k' or R may generally be assumed to remain constant over a 24 hour period, further accuracy

in the continuous determination of Q may be obtained by intermittently (e.g., every four hours) recalculating k' or R by, for example, making another thermodilution cardiac output determination or by determining cardiac output via other invasive or non-invasive means. Continuous measurements of Q are then resumed based upon the new value of R. Recalculating k' or R in this manner would also correct for any instrumentation drifts that might have occurred over the time period.

The embodiments described above continuously monitor S_aO_2 to obtain a current value for use in the modified Fick equation. However, this is not always necessary. In certain patients, who are well oxygenated and have no lung disease (e.g., cardiac patients) it may not be necessary to continuously monitor S_aO_2 since this is a constant (e.g., 96% to 98%). A single initial arterial blood sample will therefore suffice to determine the S_aO_2 value for use in the modified Fick equation. In this case, equations 7 and 9 have S_aO_2 equal to a constant, and Q can be determined by continuously monitoring VCO_2 and S_vO_2 once k or k' (together with Hgb) is determined as described above.

WHAT IS CLAIMED IS:

1. A method of continuous monitoring of the cardiac output of a patient comprising the steps of:

determining a value of a cardiac output constant for the patient by measuring at least one parameter of the patient and calculating the cardiac output constant as a function of the measured parameter;

continuously monitoring carbon dioxide production and mixed venous oxygen saturation of the patient to obtain current values thereof; and

monitoring cardiac output of the patient over time by calculating a value of cardiac output as a function of the current values of carbon dioxide production and mixed venous oxygen saturation and the previously calculated value of the cardiac output constant.

2. The method of claim 1 including the step of continuously monitoring arterial oxygen saturation of the patient to obtain a current value thereof, wherein the value of cardiac output is calculated as a function of the current value of arterial oxygen saturation and the current values of carbon dioxide production and mixed venous oxygen saturation.

3. The method of claim 1 wherein the cardiac output constant includes a gas exchange ratio R as a component thereof, where R is equal to the ratio of carbon dioxide production of the patient to oxygen intake of the patient.

4. The method of claim 3 wherein the step of determining the value of the cardiac output constant includes the steps of obtaining arterial and venous blood samples from the patient, determining the relative concentrations of oxygen and carbon dioxide in each of the samples and determining the cardiac output constant as a function of the determined concentrations.

5. The method of claim 4 including the step of determining R, wherein R is determined in accordance with the equation $R=(c_vCO_2-c_aCO_2)/(c_aO_2-c_vO_2)$, where c_vCO_2 and c_vO_2 are respectively the carbon dioxide and oxygen contents of the venous blood sample and c_aCO_2 and c_aO_2 are respectively the carbon dioxide and oxygen contents of the arterial blood sample.

6. The method of claim 3 wherein the step of determining the cardiac output constant includes the step of measuring values of the oxygen intake and carbon dioxide output of the patient, calculating R as a function of the measured values, and calculating the cardiac output constant as a function of the calculated value of R.

7. The method of claim 1 wherein the step of determining the value of the cardiac output constant includes the step of making an initial measurement of cardiac output of the patient by means of a first technique and calculating the constant as a function of the initial value of cardiac output.

8. The method of claim 7 including the step of making at least an initial measurement of arterial oxygen saturation of the patient, wherein the step of determining the value of the cardiac output constant includes the step of calculating the constant as a function of the initial value of cardiac output and initial values of carbon dioxide production, arterial oxygen saturation and mixed venous oxygen saturation.

9. The method of claim 8 including the step of determining R wherein R is determined substantially in accordance with the equation $R = VCO_2/(13.4 \cdot Hgb \cdot Q \cdot (S_aO_2 - S_vO_2))$ where VCO_2 is volume of carbon dioxide exhaled per unit time by the patient, Hgb is hemoglobin of the patient, Q is cardiac output of the patient in volume per unit time as obtained by the initial measurement, S_aO_2 is the initial value of arterial oxygen saturation and S_vO_2 is the initial value of mixed venous oxygen saturation.

10. The method of claim 1 wherein the cardiac output constant includes a value of hemoglobin of the patient as a component thereof.

11. The method of claim 1 including the step of monitoring hemoglobin value of the patient over time and calculating the cardiac output value as a function of the monitored hemoglobin values.

12. The method of claim 2 including the step of monitoring oxygen transport of the patient over time by determining a value thereof as a function of the cardiac output constant and at least one of said current values.

13. The method of claim 12 including the step of displaying a value of oxygen transport over time.

14. The method of claim 8 including step of monitoring oxygen consumption of the patient from the calculated value of R and the carbon dioxide production.

15. The method of claim 14 including the step of displaying a value of oxygen consumption over time.

16. A method of continuously monitoring cardiac output of a patient comprising the steps of:

determining an initial value of cardiac output (Q) in volume per unit time of the patient by employing a first technique;

determining initial values of carbon dioxide production (VCO_2) in volume per unit time, percentage of arterial oxygen saturation (S_aO_2) and percentage of mixed venous oxygen saturation (S_vO_2) of the patient;

calculating a value for a constant k employing the initial values of Q, VCO_2, S_aO_2 and S_vO_2, where $k = VCO_2/(Q(S_aO_2 - S_vO_2))$;

thereafter continuously determining current values of VCO_2, S_aO_2 and S_vO_2; and

calculating a current value of Q employing the calculated value of k and the current values of VCO_2, S_aO_2 and S_vO_2, where $Q = VCO_2/(k(S_aO_2 - S_vO_2))$.

17. The method of claim 16 wherein the first technique is an indicator dilution technique.

18. The method of claim 17 wherein the indicator dilution technique is a thermodilution technique.

19. The method of claim 16 wherein the initial and current values of VCO_2 are determined by measuring the fractional concentration of CO_2 in gas expired by the patient and measuring the volume of gas expired by the patient.

20. The method of claim 16 wherein initial and current values of S_aO_2 are determined by employing an oximeter to measure values of S_aO_2.

21. The method of claim 16 wherein the initial and current values of S_vO_2 are determined by employing a fiberoptic right heart catheter to measure values of S_vO_2.

22. The method of claim 16 including the step of providing a fiberoptic right heart catheter for use in determining S_vO_2.

23. The method of claim 22 wherein the first technique is a thermodilution technique and wherein the catheter includes a thermistor which is employed for temperature sensing in conjunction with the thermodilution technique.

24. Apparatus for continuously determining cardiac output in volume per unit time of a patient comprising:

first means for monitoring the volume of carbon dioxide expired by the patient per unit time and generating a first signal representing the current value thereof;

second means for monitoring the arterial oxygen saturation of the patient and generating a second signal representative of the current value thereof;

third means for monitoring the mixed venous oxygen saturation of the patient and providing a third signal representative of the current value thereof; and

processing means for receiving the first, second and third values and (a) intially calculating a cardiac output constant as a function of at least one measured parameter of the patient and (b) thereafter calculating a current value of cardiac output of the patient as a function of the cardiac output constant and the current values of the first, second and third signals.

25. The apparatus of claim 24 wherein the processing means calculates current cardiac output substantially in accordance with the equation $Q = VCO_2/(k(S_aO_2 - S_vO_2))$, where Q is cardiac output, VCO_2 is volume of carbon dioxide expired by the patient per unit time, k is the calculated cardiac output constant of the patient, S_aO_2 is the current value of the arterial oxygen concentration of the patient and S_vO_2 is the current value of mixed venous oxygen concentration of the patient.

26. The apparatus of claim 24 wherein the processing means calculates the cardiac output constant as a function of an initial measurement of cardiac output of the patient and initial values of the first, second and third signals.

27. The apparatus of claim 24 wherein the third means is a fiberoptic right heart catheter.

28. The apparatus of claim 24 wherein the first means is comprised of flow measurement means to measure the flow of gas expired by the patient and analyzer means to measure the fractional concentration of carbon dioxide in gas expired by the patient.

29. The apparatus of claim 24 including display means displays cardiac output as a function of time.

30. The apparatus of claim 27 wherein the processing means calculates the cardiac output constant as a function of values of arterial and mixed venous concentrations of both carbon dioxide and oxygen obtained by analyzing blood samples of the patient.

AMENDED CLAIMS
[received by the International Bureau
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original claims 1,3,7,9,14,24,26,29 amended;
new claims 31-33 added;other claims unchanged (8 pages)]

1. A method of continuous monitoring of the cardiac output of a patient comprising the steps of:

determining a value of a cardiac output constant for the patient by measuring at least one parameter of the patient and calculating the cardiac output constant as a function of the measured parameter, wherein the cardiac output constant is calculated without employing any assumed ratio between oxygen intake and carbon dioxide production by the patient;

continuously monitoring carbon dioxide production and mixed venous oxygen saturation of the patient to obtain current values thereof; and

monitoring cardiac output of the patient over time by calculating a value of cardiac output as a function of the current values of carbon dioxide production and mixed venous oxygen saturation and the previously calculated value of the cardiac output constant.

2. The method of claim 1 including the step of continuously monitoring arterial oxygen saturation of the patient to obtain a current value thereof, wherein the value of cardiac output is calculated as a function of the current value of arterial oxygen saturation and the current values of carbon dioxide production and mixed venous oxygen saturation.

3. The method of claim 1 wherein the cardiac output constant includes an actual gas exchange ratio R of the patient as a component thereof, where R is equal to the ratio of carbon dioxide production of the patient to oxygen intake of the patient.

4. The method of claim 3 wherein the step of determining the value of the cardiac output constant includes the steps of obtaining arterial and venous blood samples from the patient, determining the relative concentrations of oxygen and carbon dioxide in each of the samples and determining the cardiac output constant as a function of the determined concentrations.

5. The method of claim 4 including the step of determining R, wherein R is determined in accordance with the equation $R = (c_vCO_2-c_aCO_2)/(c_aO_2-c_vO_2)$, where c_vCO_2 and c_vO_2 are respectively the carbon dioxide and oxygen contents of the venous blood sample and c_aCO_2 and c_aO_2 are respectively the carbon dioxide and oxygen contents of the arterial blood sample.

6. The method of claim 3 wherein the step of determining the cardiac output constant includes the step of measuring values of the oxygen intake and carbon dioxide output of the patient, calculating R as a function of the measured values, and calculating the cardiac output constant as a function of the calculated value of R.

7. A method of continuous monitoring of the cardiac output of a patient comprising the steps of:

determining a value of a cardiac output constant for the patient by measuring at least one parameter of the patient and calculating the cardiac output constant as a function of the measured parameter wherein the step of determining the value of the cardiac output constant includes the step of making an initial measurement of cardiac output of the patient by means of a first technique and calculating the constant as a function of the initial value of cardiac output;

continuously monitoring carbon dioxide production and mixed venous oxygen saturation of the patient to obtain current values thereof; and

monitoring cardiac output of the patient over time by calculating a value of cardiac output as a function of the current values of carbon dioxide production and mixed venous oxygen saturation and the previously calculated value of the cardiac output constant.

8. The method of claim 7 including the step of making at least an initial measurement of arterial oxygen saturation of the patient, wherein the step of determining the value of the cardiac output constant includes the step of calculating the constant as a function of the initial value of cardiac output and initial values of carbon dioxide production, arterial oxygen saturation and mixed venous oxygen saturation.

9. The method of claim 8 including the step of determining the value of a respiratory quotient R wherein R is determined substantially in accordance with the equation $R = VCO_2/(13.4 \cdot Hgb \cdot Q \cdot (S_aO_2 - S_vO_2))$ where VCO_2 is volume of carbon dioxide exhaled per unit time by the patient, Hgb is hemoglobin of the patient, Q is cardiac output of the patient in volume per unit time as obtained by the initial measurement, S_aO_2 is the initial value of arterial oxygen saturation and S_vO_2 is the initial value of mixed venous oxygen saturation.

10. The method of claim 1 wherein the cardiac output constant includes a value of hemoglobin of the patient as a component thereof.

11. The method of claim 1 including the step of monitoring hemoglobin value of the patient over time and calculating the cardiac output value as a function of the monitored hemoglobin values.

12. The method of claim 2 including the step of monitoring oxygen transport of the patient over time by determining a value thereof as a function of the cardiac output constant and at least one of said current values.

13. The method of claim 12 including the step of displaying a value of oxygen transport over time.

14. The method of claim 9 including the step of monitoring oxygen consumption of the patient from the calculated value of R and the carbon dioxide production.

15. The method of claim 14 including the step of displaying a value of oxygen consumption over time.

22. The method of claim 16 including the step of providing a fiberoptic right heart catheter for use in determining S_vO_2.

23. The method of claim 22 wherein the first technique is a thermodilution technique and wherein the catheter includes a thermistor which is employed for temperature sensing in conjunction with the thermodilution technique.

24. Apparatus for continuously determining cardiac output in volume per unit time of a patient comprising:

first means for monitoring the volume of carbon dioxide expired by the patient per unit time and generating a first signal representing the current value thereof;

second means for monitoring the arterial oxygen saturation of the patient and generating a second signal representative of the current value thereof;

third means for monitoring the mixed venous oxygen saturation of the patient and providing a third signal representative of the current value thereof; and

processing means for receiving the first, second and third values and (a) initially calculating a cardiac output constant as a function of at least one measured parameter of the patient without employing any assumed ratio between oxygen intake and carbon dioxide production for the patient and (b) thereafter calculating a current value of cardiac output of the patient as a function of the cardiac output constant and the current values of the first, second and third signals.

25. The apparatus of claim 24 wherein the processing means calculates current cardiac output substantially in accordance with the equation $Q = VCO_2/(k(S_aO_2 - S_vO_2))$, where Q is cardiac output, VCO_2 is volume of carbon dioxide expired by the patient per unit time, k is the calculated cardiac output constant of the patient, S_aO_2 is the current value of the arterial oxygen concentration of the patient and S_vO_2 is the current value of mixed venous oxygen concentration of the patient.

26. Apparatus for continuously determining cardiac output in volume per unit time of a patient comprising:

first means for monitoring the volume of carbon dioxide expired by the patient per unit time and generating a first signal representing the current value thereof;

second means for monitoring the arterial oxygen saturation of the patient and generating a second signal representative of the current value thereof;

third means for monitoring the mixed venous oxygen saturation of the patient and providing a third signal representative of the current value thereof; and

processing means for receiving the first, second and third values and (a) initially calculating a cardiac output constant as a function of at least one measured parameter of the patient, wherein the processing means calculates the cardiac output constant as a function of an initial measurement of cardiac output of the patient and initial values of the first, second and third signals and (b) thereafter calculating a current value of cardiac output of the patient as a function of the cardiac output constant and the current values of the first, second and third signals.

27. The apparatus of claim 24 wherein the third means is a fiberoptic right heart catheter.

28. The apparatus of claim 24 wherein the first means is comprised of flow measurement means to measure the flow of gas expired by the patient and analyzer means to measure the fractional concentration of carbon dioxide in gas expired by the patient.

29. The apparatus of claim 24 including display means which displays cardiac output as a function of time.

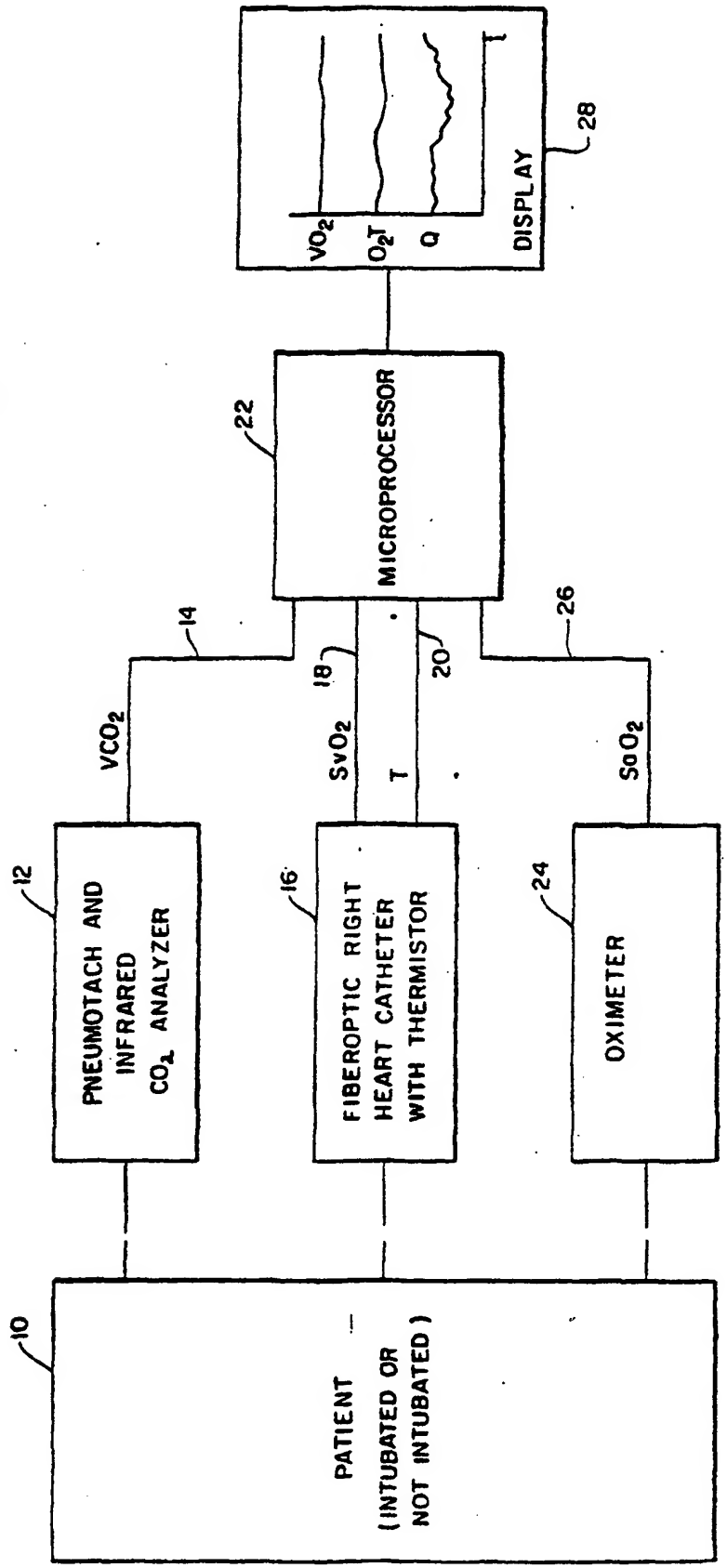
30. The apparatus of claim 27 wherein the processing means calculates the cardiac output constant as a function of values of arterial and mixed venous concentrations of both carbon dioxide and oxygen obtained by analyzing blood samples of the patient.

31. The method of claim 1 including the step of displaying the value of cardiac output over time.

32. The apparatus of claim 29 wherein the processing means includes means for calculating a current value of oxygen transport of the patient and the display means displays the calculated values of oxygen transport over time.

33. The apparatus of claim 29 wherein the processing means includes means for calculating a current value of oxygen consumption of the patient and the display means displays the calculated values of oxygen consumption over time.

FIG. 1


PATIENT
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PNEUMOTACH AND
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CO_2 ANALYZER
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FIBEROPTIC RIGHT
HEART CATHETER
WITH THERMISTOR
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OXIMETER
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SvO_2
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MICROPROCESSOR
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VO_2
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DISPLAY
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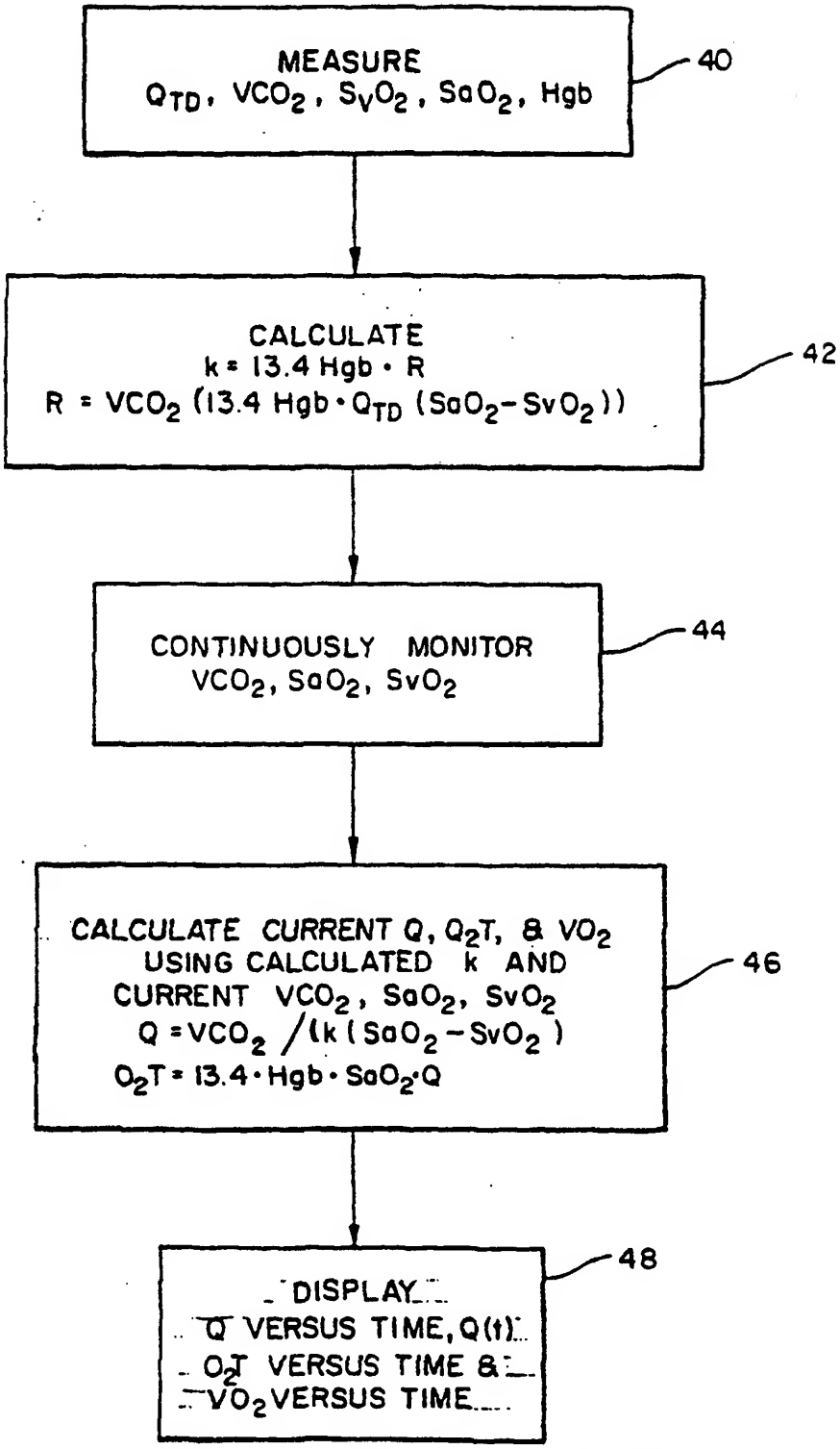
FIG. 2



SUBSTITUTE SHEET

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US89/05765

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

INT. CL. (5) A61N 1/08 U.S. CL. 128/713

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
U.S.	CLASS: 128, SUBCLASS 713, 670, 671, 691, 719, 633, 634

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No [13]
Y	CRIT. Care Med., Vol. 14, No. 881, 1986, DAVIES G.G. ET AL. "Continuous Flick Cardiac Output Compared to Dilution Cardiac Output". See entire document.	1-30
Y	CritCare Med. (Abstract), Vol. 14, No. 4 , 1986. TACHIMORI Y. ET AL., "On line Monitoring System for continuous and Real-time Cardiac Output. See entire document.	1-30
Y	Crit. Care Med., Vol. 16 No. 8, August 1988, VAN LANSCHOT ET AL., "Accuracy of intermittent Metabolic Gas Exchange of Recordings Extrapolated for Diurnal Variation", pp. 737-741.	3-6

* Special categories of cited documents: [14]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
31 January 1990	16 MAR 1990
International Searching Authority	**Signature of Authorized Officer**
ISA/US	S. Getzow - Scott Getzow

Form PCT/ISA/210 (second sheet) (Rev. 11-87)

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

Y	ANN BIOMED ENG. VOL. 14, NO. 219, 1986, EHLERS K, C. ET AL., "Cardiac Output Measurements a Review of Techniques and Research": See entire document.	23
Y	Datascope Technical Reference, 27 OCTOBER 1983. See entire document.	29

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE [1]

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers . because they relate to subject matter [12] not required to be searched by this Authority, namely:

2. ☐ Claim numbers . because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out [13], specifically:

3. ☐ Claim numbers_____, because they are dependent claims not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING [2]

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:

4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

☐ The additional search fees were accompanied by applicant's protest.

☐ No protest accompanied the payment of additional search fees.